The effect of mechanical properties on the dynamics of micro-aggregation quantified using a deformable cell-based model

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The three-dimensional nature of tissue establishes a biophysical environment which regulates auto- and paracrine signalling and affects both cell function and cell fate. 3D Micro-tissues provide an *in vitro* tool that is excellently suited to study the biology of small multicellular systems [1]. In micro-well aggregation, cells are seeded on a non-adhesive substrate such as agarose where they naturally form compact spherical three-dimensional aggregates. The formation of these aggregates is characterized by two phases. First, the cells actively migrate towards each other to form a loose cluster of cells. Next, the clusters condensate into smooth, spherical micro-aggregates.

From a physical point of view, the transition from a cell monolayer towards 3D aggregates can be considered as a 'de-wetting' process. This process is affected by the mechanics of cell-substrate interaction and the active mechanical behaviour of the cell. In this study, we developed a cell-based computational model which simulates the dynamics of micro-well cell aggregation. We construct a phase-diagram of this system, which predicts 3D aggregation as a function of cell-substrate adhesion, contractility and cell motility (see Figure 1). Furthermore, we investigate the effect of the most important mechanical parameters on the final shape of the cell aggregates, individual cell morphology and the general characteristics of the mechanical micro-environment.

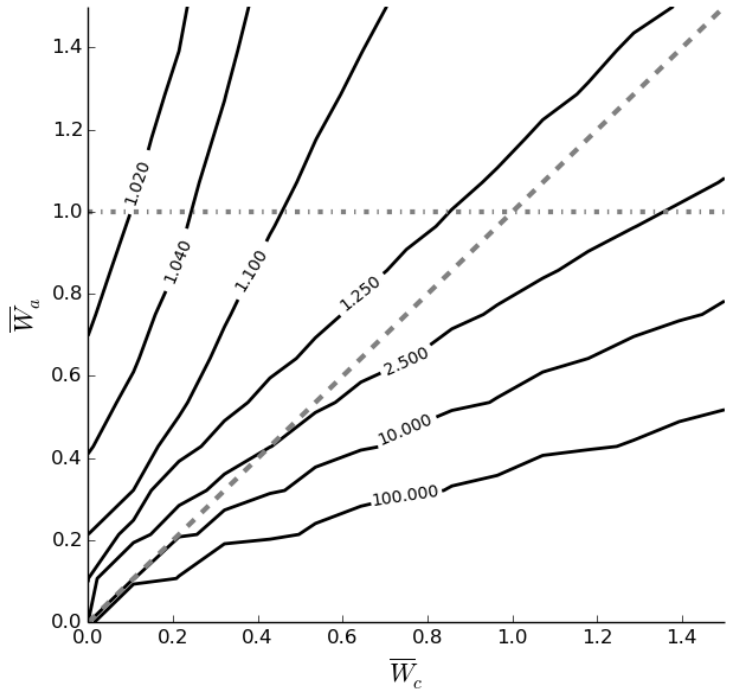

Figure 1: “de-wetting” map with iso-lines of 2D relative density (cells / surface area) for varying relative cell-substrate adhesion energy and cell-cell contractility (Wa and Wc). High densities indicate de-wetting.

[1] Moreira Teixeira, L. S., et al. "High throughput generated micro-aggregates of chondrocytes stimulate cartilage formation in vitro and in vivo." European cells & materials 23 (2012): 387-399.